A Lissencephaly-1 homologue is essential for mitotic progression in the planarian Schmidtea mediterranea.

Journal: Dev Dyn

Publication Year: 2012

Authors: Martis W Cowles, Amy Hubert, Ricardo M Zayas

PubMed link: 22411224

Funding Grants: The molecular basis underlying adult neurogenesis during regeneration and tissue renewal

Public Summary:
Lissencephaly-1, which is implicated in human diseases, is a protein required for normal cell division. In this study we examine the role of Lissencephaly-1 in the freshwater planarian Schmidtea mediterranea. The animals possess a high concentration of mitotic cells and provide an excellent opportunity to examine the role of proteins, such as Lissencephaly-1, in stem cell division. We show that Lissencephaly-1 is essential for mitotic progression in planarian stem cells and establish the system for future studies aimed at investigating signaling roles of Lissencephaly-1 implicated in stem cell regulation.

Scientific Abstract:
BACKGROUND: Planarians are renowned for their capacity to replace lost tissues from adult pluripotent stem cells (neoblasts). Here we report that Lissencephaly-1 (lis1), which has roles in cellular processes such as mitotic spindle apparatus orientation and in signal regulation required for stem cell self-renewal, is required for stem cell maintenance in the planarian Schmidtea mediterranea. RESULTS: In planarians, lis1 is expressed in differentiated tissues and stem cells. lis1 RNAi leads to head regression, ventral curling, and death by lysis. By labeling the neoblasts and proliferating cells, we found lis1 knockdown animals show a dramatic increase in the number of mitotic cells, followed by depletion of the stem cell pool. Analysis of the mitotic spindles in dividing neoblasts revealed that defective spindle positioning is correlated with cells arrested at metaphase. In addition, we show that inhibiting a planarian homologue of nudE, predicted to encode a LIS-1 interacting protein, also leads to cell cycle progression defects. CONCLUSIONS: Our results provide evidence for a conserved role of LIS1 and NUDE in regulating the function of the mitotic spindle apparatus in a representative Lophotrochozoan and that planarians will be useful organisms in which to investigate LIS1 regulation of signaling events underlying stem cell self-renewal.